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[Continued on next page]

(54) Title: METHOD FOR IDENTIFYING COMPOUNDS THAT AFFECT EXPRESSION OF TRYPTOPHAN HYDROXY-LASE ISOFORM 2

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mTPH2: MOPAMMFSSKYWARRGLSLDSAPVEDHOLLGSLTONKATKSEDKKSGKEPGKGDTE
mTPH1: M.....I...EDNKENKEN.KDHSSE

mTPH2: SSKTAVVFLKNEVGGLVKALRLFOEKHVNMLHIESRRSRSSSEVEIFVDCCEGKTE
mTPH1: RGRVTLIFSLNEVGGLIKVLKIFQENHVSLLHIESRKSQRNSEFEIFVDCDTSREQ

*****
mTPH2: FNELTQLLKFTTIVTLNPPESIWTTEEEDLEVPWFPRKISELDRCSHRVLMYGTELD
mTPH1: LNDIFPLLKSHATVLSVDSPOQLTAKEDVMEIVPWFPKISLDLFCANRVLLYGSELD

mTPH2: ADHPGFKDNYRQRKYFVDVAMGYKYGQPIPRVEYTEETKTWGVFREL SKLYPTH
mTPH1: ADHPGFKDNYRQRKYFAELAMNYKHGDIPIKIEFTEETKTWGTIFRELNLKLYPTH

mTPH2: ACREYLKNIPLLLTKYCYREDNPQLEDVSMFLKERSGFTVRPVAGYLSPRDFLAGLA
mTPH1: ACREYLRNLPLLSKYCYREDNIPQLEDVSNFLKERTGFSIRPVAGYLSPRDFLSGLA

mTPH2: YRVFHTQYVRHGSDDPLYTPEPDTCHELLGHVPLLADPKFAQFSOEIGLASLGASDED
mTPH1: FRVFHTQYVRHGSDDPLYTPEPDTCHELLGHVPLLAEPSFAQFSOEIGLASLGASEET

*****
mTPH2: VQKLATCYFFTIEFGLCKQEQQLRAYGAGLLSSIGELKHALSDKACVKSFPDPTTCLQ
mTPH1: VQKLATCYFFTIEFGLCKQEQQLRVFGAGLLSSISELKHALSGHAKVKPFPDPTACKQ

mTPH2: ECLITTFQDAYFVSDSFEAAKEKMRDFAKSIIRPFVYFVRYTOSIEILKDRSIEV
mTPH1: ECLITSFQDAYFVSEFEDAKEKMRFAKTVKRPFGKYNPYTOSVQVLRDTSITSA

mTPH2: VQDLRSDLTVC DALNKQNYLGI
mTPH1: MNELRYDLVDISDALARVTRMPSV

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Light Text = Identity between sequences (68 %)

----- = TPH2a ISH probe

----- = TPH2b ISH probe

----- = TPH1-892 ISH probe

Underlined residues = TPH2c ISH probe

***** = Real-time RT-PCR amplicons

= Catalytic domain

(57) Abstract: A method for identifying analytes which directly or indirectly affect tryptophan hydroxylase isoform 2 (TPH2) expression is described. The method enables glucocorticoid receptor modulators and α -hydroxysteroid dehydrogenase type 1 (α -HSD1) inhibitors to be screened for central nervous system penetrance and activity by determining their ability to regulate expression of TPH2. The method is particularly useful for identifying analytes which suppress glucocorticoid disruption of central serotonergic neurotransmission in the brain.



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.